

CLAIMS

1. A recombinant or isolated integrin subunit $\alpha 11$
comprising essentially the amino acid sequence shown in
5 SEQ ID No. 1, and homologues and fragments thereof.

2. A process of producing a recombinant integrin
subunit $\alpha 11$ comprising essentially the amino acid
sequence shown in SEQ ID No. 1, and homologues and
fragments thereof, which process comprises the steps of

10 a) isolating a polynucleotide comprising a nucleo-
tide sequence coding for a integrin subunit $\alpha 11$, of for
homologues and fragments thereof,

b) constructing an expression vector comprising the
isolated polynucleotide,

15 c) transforming a host cell with said expression
vector,

d) culturing said transformed host cell in a culture
medium under conditions suitable for expression of said
integrin subunit $\alpha 11$, of said homologues and fragments,
20 in said transformed host cell, and, optionally,

e) isolating the integrin subunit $\alpha 11$, or homologues
and fragments thereof, from said transformed host cell or
said culture medium.

3. A process according to claim 2, step c, said
25 transforming being an *in vitro* or *in situ* process.

4. A process according to claim 2, step c, said
transforming being an *in vivo* process.

5. A process of providing an integrin subunit $\alpha 11$,
or homologues or fragments thereof, as defined in claim
30 1, whereby said subunit is isolated from a cell in which
it is naturally present.

6. An isolated polynucleotide or oligonucleotide
comprising a nucleotide coding for an integrin subunit
 $\alpha 11$, or for homologues or fragments thereof, which
35 polynucleotide or oligonucleotide comprises essentially
the nucleotide sequence shown in SEQ ID No. 1 or suitable
parts thereof.

7. An isolated polynucleotide or oligonucleotide which hybridises to a polynucleotide or oligonucleotide as defined in claim 4, whereby said isolated polynucleotide or oligonucleotide fails to hybridise to a polynucleotide or oligonucleotide encoding an integrin subunit $\alpha 10$.

8. A vector comprising a polynucleotide or oligonucleotide as defined in claim 6 or 7.

9. A cell containing the vector as defined in claim 8.

10. A cell, as generated by the process in steps a) to c) of claim 2, in which a polynucleotide or oligonucleotide coding for an integrin subunit $\alpha 11$, or for homologues and fragments thereof, said polynucleotide or oligonucleotide comprising essentially the nucleotide sequence shown in SEQ ID No. 1 or parts thereof, has been stably integrated in the cell genome.

11. Binding sites of the amino acid sequence of the integrin subunit $\alpha 11$, or of homologues and fragments thereof, as defined in claim 1, said binding sites having the capability of binding specifically to entities chosen from the group comprising proteins, peptides, carbohydrates, lipids, natural integrin binding ligands, polyclonal and monoclonal antibodies, and fragments thereof.

12. Binding entities having the capability of binding specifically to integrin subunit $\alpha 11$, or to homologues or fragments thereof, as defined in claim 1, which entities are chosen from the group comprising proteins, peptides, carbohydrates, lipids, natural integrin binding ligands, polyclonal and monoclonal antibodies, and fragments thereof.

13. A recombinant or isolated integrin heterodimer comprising a subunit $\alpha 11$ and a subunit β , in which the subunit $\alpha 11$ comprises essentially the amino acid sequence shown in SEQ ID No. 1 or homologues or fragments thereof.

14. A recombinant or isolated integrin heterodimer according to claim 11, wherein the subunit β is β_1 .

15. A process of producing a recombinant integrin heterodimer comprising a subunit α_{11} and a subunit β , in which the subunit α_{11} comprises essentially the amino acid sequence shown in SEQ ID No. 1, or homologues or fragments thereof, which process comprises the steps of

a) isolating one polynucleotide or oligonucleotide comprising a nucleotide sequence coding for said subunit α_{11} of said integrin heterodimer, or for said homologues or fragments thereof, and, optionally, another polynucleotide comprising a nucleotide sequence coding for said subunit β of an integrin heterodimer, or for homologues or fragments thereof,

b) constructing an expression vector comprising said isolated polynucleotides or oligonucleotides

c) transforming a host cell with said expression vector or vectors,

d) culturing said transformed host cell in a culture medium under conditions suitable for expression of said integrin heterodimer, or said homologues or fragments thereof, in said transformed host cell, and, optionally,

e) isolating said integrin heterodimer, or said homologues or fragments thereof, from said transformed host cell or said culture medium.

16. A process according to claim 15, step c, said transforming being an *in vitro* process.

17. A process according to claim 15, step c, said transforming being an *in vivo* process.

18. A process of providing an integrin heterodimer comprising a subunit α_{11} and a subunit β , as defined in claim 13 or 14, or homologues or fragments thereof, whereby said integrin heterodimer is isolated from a cell in which it is naturally present.

19. A cell containing

i) a first vector, said first vector comprising a polynucleotide or oligonucleotide coding for a subunit

α 11 of an integrin heterodimer, or for homologues or fragments thereof, which polynucleotide or oligonucleotide comprises essentially the nucleotide sequence shown in SEQ ID No. 1 or parts thereof, and

- 5 ii) a second vector, said second vector comprising a polynucleotide or oligonucleotide coding for a subunit β of said integrin heterodimer.

20. Binding sites of an integrin heterodimer as defined in claim 13 or 14, or of homologues or fragments
 10 thereof, said binding sites having the capability of binding specifically to entities chosen among the group comprising proteins, peptides, carbohydrates, lipids, natural integrin binding ligands, polyclonal and monoclonal antibodies, and fragments thereof.

15 21. Binding entities having the capability of binding specifically to an integrin heterodimer as defined in claim 13 or 14, or to homologues or fragments thereof, said binding entities being chosen among the group comprising proteins, peptides, carbohydrates, lipids,
 20 natural integrin binding ligands, polyclonal and monoclonal antibodies, and fragments thereof.

22. A fragment of an integrin subunit α 11, which integrin subunit α 11 comprises essentially the amino acid sequence shown in SEQ ID NO: 1, said fragment being a
 25 peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the extracellular extension region.

23. A fragment according to claim 22, said fragment being a peptide from the cytoplasmic domain comprising
 30 essentially the amino acid sequence
 KLGFFRSARRRREPGLDPTPKVLE.

24. A fragment according to claim 22, which is a peptide comprising essentially the amino acid sequence of the extracellular domain, from about amino acid No. 804
 35 to about amino acid no. 826 of SEQ ID No. 1.

25. A fragment according to claim 22, which is a peptide comprising essentially the amino acid sequence of

the I-domain, from about amino acid No. 159 to about amino acid no. 355 of SEQ ID No. 1.

26. A method of producing a fragment of the integrin subunit $\alpha 11$ as defined in any one of claims 22-25, which
5 method comprises a sequential addition of amino acids.

27. A polynucleotide or oligonucleotide coding for a fragment of the integrin subunit $\alpha 11$ as defined in any one of claims 22-25.

28. Binding sites of an integrin subunit $\alpha 11$
10 fragment as defined in any one of claims 22-25, said binding sites having the capability of binding specifically to entities chosen from the group comprising proteins, peptides, carbohydrates, lipids, natural
integrin binding ligands, monoclonal and polyclonal
15 antibodies, and fragments thereof.

29. Binding entities having the capability of binding specifically to an integrin subunit $\alpha 11$ fragment as defined in any one of claims 22-25, which binding entities are chosen from the group comprising proteins,
20 peptides, carbohydrates, lipids, natural integrin binding ligands, monoclonal and polyclonal antibodies, and fragments thereof.

30. A process of using an integrin subunit $\alpha 11$ comprising essentially the amino acid sequence shown in SEQ
25 ID No.1 or an integrin heterodimer comprising said subunit $\alpha 11$ and a subunit β , or homologues or fragments thereof, as a marker or target molecule of cells or tissues expressing said integrin subunit $\alpha 11$, which cells or tissues are of animal including human origin.

30 31. A process according to claim 30, which is a process for determining the differentiation-state of cells during differentiation, development, in pathological conditions, in tissue regeneration, in transplantation, or in therapeutic and physiological
35 reparation of tissues.

32. A process according to claim 31, which process is used during pathological conditions involving said subunit $\alpha 11$.

5 33. A process according to claim 31, which pathological conditions are comprised within the group comprising damage of muscles, muscle dystrophy, fibrosis and wound healing.

10 34. A process according to claim 31, which pathological conditions are comprised within the group comprising damage of cartilage and/or bone, and cartilage and/or bone diseases.

15 35. A process according to claim 31, which pathological conditions are comprised within the group comprising trauma, rheumatoid arthritis, osteoarthritis and osteoporosis.

36. A process according to claim 30, which is a process for detecting the formation of cartilage during embryonic development.

20 37. A process according to claim 30, which is a process for detecting physiological or therapeutic repair of cartilage and/or muscle.

25 38. A process according to claim 30, which is a process for selection and analysis, or for sorting, isolating or purification of chondrocytes and/or muscle cells.

30 39. A process according to claim 30, which is a process for detecting regeneration of cartilage or chondrocytes during transplantation of cartilage or chondrocytes, respectively, or of muscle or muscle cells during transplantation of muscle or muscle cells, respectively.

40. A process according to claim 30, which is a process for studies of differentiation of chondrocytes or muscle cells.

35 41. A process according to any one of claims 30-40, which is an *in vitro* process.

42. A process according to any one of claims 30-40, which is an *in situ* process.

43. A process according to any one of claims 30-40, which is an *in vivo* process.

5 44. A process according to any one of claims 30-43, whereby a fragment of said integrin subunit $\alpha 11$ is a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the extracellular extension region.

10 45. A process according to claim 44, whereby said fragment is a peptide comprising essentially the amino acid sequence KLGFFRSARRRREPGLDPTPKVLE from the cytoplasmic domain.

15 46. A process according to claim 44, whereby said fragment is a peptide comprising essentially the amino acid sequence of the extracellular domain, from about amino acid No. 804 to about amino acid no. 826 of SEQ ID No. 1.

20 47. A process according to claim 44, whereby said fragment is a peptide comprising essentially the amino acid sequence of the I-domain, from about amino acid No. 159 to about amino acid no. 355 of SEQ ID No. 1.

48. A process according to any one of claims 30-47, whereby a subunit β of the integrin heterodimer is $\beta 1$.

25 49. A process according to claim 30, whereby said cells are chosen from the group comprising fibroblasts, muscle cells, chondrocytes, osteoblasts, mesenchymally derived cells and stem cells.

30 50. A process of using binding entities having the capability of binding specifically to binding sites of an integrin subunit $\alpha 11$ comprising essentially the amino acid sequence shown in SEQ ID No. 1, or an integrin heterodimer comprising said subunit $\alpha 11$ and a subunit β , or to homologues or fragments thereof, as markers or
35 target molecules of cells or tissues expressing said integrin subunit $\alpha 11$, which cells or tissues are of animal including human origin.

51. A process according to claim 50, which is a process for detecting the presence of an integrin subunit $\alpha 11$ comprising essentially the amino acid sequence shown in SEQ ID No. 1, or of an integrin heterodimer comprising
5 said subunit $\alpha 11$ and a subunit β , or of homologues or fragments thereof.

52. A process according to claim 50, which is a process for determining the differentiation-state of cells during differentiation, development, in
10 pathological conditions, in tissue regeneration, in transplantation, or in therapeutic and physiological repair of tissues.

53. A process according to claim 52, which process is used during pathological conditions involving said
15 subunit $\alpha 11$.

54. A process according to claim 52, which pathological conditions are comprised within the group comprising damage of muscles, muscle dystrophy, fibrosis and wound healing.

20 55. A process according to claim 52, which pathological conditions are comprised within the group comprising damage of cartilage and/or bone, and cartilage and/or bone diseases.

25 56. A process according to claim 52, which pathological conditions are comprised within the group comprising trauma, rheumatoid arthritis, osteoarthritis and osteoporosis.

30 57. A process according to claim 52 which is a process for detecting the formation of cartilage during embryonic development.

58. A process according to claim 52, which is a process for detecting physiological or therapeutic reparation of cartilage and/or muscle.

35 59. A process according to claim 52, which is a process for selection and analysis, or for sorting, isolating or purification of chondrocytes and/or muscle cells.

60. A process according to claim 52, which is a process for detecting regeneration of cartilage or chondrocytes during transplantation of cartilage or chondrocytes, respectively, or of muscle or muscle cells during transplantation of muscle or muscle cells, respectively.

61. A process according to claim 52, which is a process for studies of differentiation of chondrocytes or muscle cells.

62. A process according to any one of claims 50-61, which is an *in vitro* process.

63. A process according to any one of claims 50-61, which is an *in situ* process.

64. A process according to any one of claims 50-61, which is an *in vivo* process.

65. A process according to any one of claims 50-61, whereby a fragment of said integrin subunit $\alpha 11$ is a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the extracellular extension region.

66. A process according to claim 65, whereby said fragment is a peptide comprising essentially the amino acid sequence KLGFFRSARRRREPGLDPTPKVLE from the cytoplasmic domain.

67. A process according to claim 65, whereby said fragment is a peptide comprising essentially the amino acid sequence of the extracellular domain, from about amino acid No. 804 to about amino acid no. 826 of SEQ ID No. 1.

68. A process according to claim 65, whereby said fragment is a peptide comprising essentially the amino acid sequence of the I-domain, from about amino acid No. 159 to about amino acid no. 355 of SEQ ID No. 1.

69. A process according to any one of claims 50-68, whereby a subunit β of the integrin heterodimer is $\beta 1$.

70. A process according to claim 50, whereby said cells are chosen from the group comprising fibroblasts,

muscle cells, chondrocytes, osteoblasts, mesenchymally derived cells and stem cells.

71. A process for detecting the presence of an integrin subunit $\alpha 11$, or of homologues or fragments of said integrin subunit, on cells, whereby a polynucleotide or oligonucleotide chosen from the group comprising a polynucleotide or oligonucleotide having essentially the nucleotide sequence as shown in SEQ ID No. 1, or homologues or fragments thereof, is used as a marker under hybridisation conditions, wherein said polynucleotide or oligonucleotide fails to hybridise to a polynucleotide or oligonucleotide encoding an integrin subunit $\alpha 10$.

72. A process according to claim 71, which is a process for determining the differentiation-state of cells during differentiation, development, in pathological conditions, in tissue regeneration, in transplantation, or in therapeutic and physiological reparation of tissues.

73. A process according to claim 72, which process is used during pathological conditions involving said subunit $\alpha 11$.

74. A process according to claim 72, which pathological conditions are comprised within the group comprising damage of muscles, muscle dystrophy, fibrosis and wound healing.

75. A process according to claim 72, which pathological conditions are comprised within the group comprising damage of cartilage and/or bone, and cartilage and/or bone diseases.

76. A process according to claim 72, which pathological conditions are comprised within the group comprising trauma, rheumatoid arthritis, osteoarthritis and osteoporosis.

77. A process according to claim 72, which is a process for detecting the formation of cartilage during embryonic development.

78. A process according to claim 72, which is a process for detecting physiological or therapeutic reparation of cartilage and/or muscle.

5 79. A process according to claim 72, which is a process for selection and analysis, or for sorting, isolating or purification of chondrocytes and/or muscle cells.

10 80. A process according to claim 72, which is a process for detecting regeneration of cartilage or chondrocytes during transplantation of cartilage or chondrocytes, respectively, or of muscle or muscle cells during transplantation of muscle or muscle cells, respectively.

15 81. A process according to claim 72, which is a process for studies of differentiation of chondrocytes or muscle cells.

82. A process according to any one of claims 71-81, which is an *in vitro* process.

20 83. A process according to any one of claims 71-81, which is an *in situ* process.

84. A process according to any one of claims 71-81, which is an *in vivo* process.

25 85. A process according to any one of claims 71-84, whereby said polynucleotide or oligonucleotide is a polynucleotide or oligonucleotide coding for a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the extracellular extension region.

30 86. A process according to claim 85, whereby said peptide is a peptide comprising essentially the amino acid sequence KLGFFRSARRRREPGLDPTPKVLE from the cytoplasmic domain.

35 87. A process according to claim 85, whereby said peptide is a peptide comprising essentially the amino acid sequence of the extracellular domain, from about amino acid No. 804 to about amino acid no. 826 of SEQ ID No. 1.

88. A process according to claim 85, whereby said peptide is a peptide comprising essentially the amino acid sequence of the I-domain, from about amino acid No. 159 to about amino acid no. 355 of SEQ ID No. 1.

5 89. A process according to any one of claims 71-88, whereby a subunit β of the integrin heterodimer is $\beta 1$.

90. A process according to claim 71, whereby said cells are chosen from the group comprising fibroblasts, muscle cells, chondrocytes, osteoblasts, mesenchymally
10 derived cells and stem cells.

91. A pharmaceutical composition comprising as an active ingredient a pharmaceutical agent or an antibody which is capable of using an integrin heterodimer comprising a subunit $\alpha 11$ and a subunit β , or the subunit $\alpha 11$
15 thereof, or homologues or fragment of said integrin or subunit $\alpha 11$, as a target molecule.

92. A pharmaceutical composition comprising as an active ingredient a pharmaceutical agent or an antibody which is capable of stimulating cell surface expression
20 or activation of an integrin heterodimer comprising a subunit $\alpha 11$ and a subunit β , or the subunit $\alpha 11$ thereof, or homologues or fragments of said integrin or subunit $\alpha 11$.

93. A pharmaceutical composition according to claim
25 92, for use in stimulating, inhibiting or blocking the formation of muscles, cartilage, bone or blood vessels.

94. A vaccine comprising as an active ingredient at least one member of the group comprising an integrin heterodimer, which heterodimer comprises a subunit $\alpha 11$
30 and a subunit β , or the subunit $\alpha 11$ thereof, and mologues or fragments of said integrin or subunit $\alpha 11$, and a polynucleotide and a oligonucleotide coding for said integrin subunit $\alpha 11$.

95. A method of gene therapy, whereby a vector
35 comprising a polynucleotide or oligonucleotide coding for a subunit $\alpha 11$ of an integrin heterodimer, or for homologues or fragments thereof, which polynucleotide or

oligonucleotide comprises essentially the nucleotide sequence shown in SEQ ID NO: 1 or parts thereof, and optionally a second vector comprising a polynucleotide or oligonucleotide coding for a subunit β of said integrin heterodimer, is administered to a subject suffering from pathological conditions involving said subunit $\alpha 11$.

96. A method of using binding entities having the capability of binding specifically to binding sites of an integrin subunit $\alpha 11$ comprising substantially the amino acid sequence shown in SEQ ID No. 1, or of an integrin heterodimer comprising said subunit $\alpha 11$ and a subunit β , or to homologues or fragments thereof, for promoting adhesion of cells.

97. A method of using an integrin heterodimer comprising an integrin subunit $\alpha 11$ and a subunit β , or the subunit $\alpha 11$ thereof, or homologues or fragments of said integrin or subunit $\alpha 11$, as a target for anti-adhesive drugs or molecules in tissues where adhesion impairs the function of the tissue.

98. A method of in vitro detecting the presence of integrin binding entities, comprising interaction of an integrin heterodimer comprising a subunit $\alpha 11$ and a subunit β , or the subunit $\alpha 11$ thereof, or homologues or fragments of said integrin or subunit, with a sample, thereby causing said integrin, subunit $\alpha 11$, or homologue or fragment thereof, to modulate the binding to its natural ligand or other integrin binding proteins present in said sample.

99. A method of in vitro studying consequences of the interaction of a human heterodimer integrin comprising a subunit $\alpha 11$ and a subunit β , or the subunit $\alpha 11$ thereof, or homologues or fragments of said integrin or subunit, with an integrin binding entity and thereby initiate a cellular reaction.

100. A method according to claim 99, whereby the consequences of said interactions are measured as alterations in cellular functions.

101. A method of using a polynucleotide or oligonucleotide encoding an integrin subunit $\alpha 11$ or homologues or fragments thereof as a target molecule.

102. A method according to claim 101, comprising
5 hybridising a polynucleotide or oligonucleotide to the DNA or RNA encoding the integrin subunit $\alpha 11$ or homologue or fragment thereof, which polynucleotide or oligonucleotide fails to hybridise to a polynucleotide or oligonucleotide encoding an integrin subunit $\alpha 10$.

10 103. A method of using binding entities having the capability of binding specifically to an integrin subunit $\alpha 11$ comprising the amino acid sequence shown in SEQ ID No. 1 or SEQ ID No. 2, or an integrin heterodimer comprising said subunit $\alpha 11$ and a subunit β , or to homologues or fragments thereof having similar biological
15 activity, for promoting adhesion of chondrocytes and/or osteoblasts to surfaces of implants to stimulate osseointegration.

104. A method of using an integrin heterodimer
20 comprising an integrin subunit $\alpha 11$ and a subunit β , or the subunit $\alpha 11$ thereof, or homologues or fragments of said integrin or subunit $\alpha 11$, as a target for anti-adhesive drugs or molecules in tendon, ligament, skeletal muscle or other tissues where adhesion impairs the
25 function of the tissue.

105. A method of stimulating, inhibiting or blocking the formation of cartilage or bone, comprising administration to a subject a suitable amount of a pharmaceutical agent or an antibody which is capable of using an
30 integrin heterodimer comprising a subunit $\alpha 11$ and a subunit β , or the subunit $\alpha 11$ thereof, or homologues or fragments of said integrin or subunit $\alpha 11$, as a target molecule.

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